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Current Practices of Screening for Incident Hepatitis C Virus (HCV) Infection Among HIV-Infected, HCV-Uninfected Individuals in Primary Care

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(See the Major Article by Vanhommerig et al on pages 1678–85, and the Editorial Commentary by Reiberger on pages 1694–5.)

Background. Human immunodeficiency virus (HIV)-infected, hepatitis C virus (HCV)-uninfected patients are at risk for incident HCV infection, but little is known about screening practices for incident HCV among HIV-infected individuals in HIV primary care clinics.

Methods. We used data from the Center for AIDS Research Network of Integrated Clinical Systems (CNICS) to investigate historical trends in screening for incident HCV infection among HIV-infected patients who were HCV-uninfected at enrollment in care. We used descriptive measures and Poisson regression to identify factors associated with screening for HCV infection (using HCV antibody or RNA), performed temporal analyses to assess changes in screening over time, and investigated the frequency with which elevated alanine aminotransferase (ALT) levels were followed by diagnostic HCV testing.

Results. Among 17 090 patients registered at CNICS sites between 2000 and 2011, 14 534 (85%) received HCV antibody screening within 3 months of enrolling in care, and 9077 met all of the inclusion criteria. Only 55.6% ever received additional HCV screening. HCV screening increased over time, but not uniformly at all sites. Only 26.7% of first-time ALT elevations to >100 IU/L were followed up within 12 months by HCV antibody or RNA testing.

Conclusions. Although most HIV-infected patients were screened for prevalent HCV infection at enrollment in care, only half who were HCV uninfected were screened again. Screening varied between sites, even when controlling for demographics and risk behaviors. Patients with new ALT elevations to >100 IU/L were seldom assessed for incident HCV infection. Guidelines are needed to help HIV providers know whom to screen, how frequently to screen, and which screening test to use.

Keywords. HIV; hepatitis C; screening; men who have sex with men; incidence.

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Hepatitis C virus (HCV) coinfection is a leading cause of hospitalization and death among human immunodeficiency virus (HIV)-infected individuals in the United States and Europe [1–3]. Prevalent HCV infection is commonly associated with a history of current or past injection drug use (IDU) [4, 5]. Patients with a history

of IDU who are not HCV infected remain at an increased risk of developing incident HCV infection [6, 7]. Furthermore, over the previous decade, cohort studies have demonstrated a rising HCV incidence among HIV-infected men who have sex with men (MSM) [7–20]. Most of these men with newly acquired HCV infection reported no history of IDU—their risk appears to be related to unprotected anal intercourse and noninjection drug use, especially amphetamines [21].

In 2010, the European AIDS Treatment Network published screening guidelines for incident HCV infection among HIV-infected individuals, recommending testing twice a year using serum alanine aminotransferase (ALT) and annually with HCV antibody (Ab) among MSM engaging in unprotected anal sex, as well as screening within 3 months of diagnosis of a new sexually transmitted infection (STI) or IDU exposure [22]. Mathematical modeling suggests that such a strategy would extend life expectancy and be cost-effective [23]. In the United States, STI guidelines published by the Centers for Disease Control and Prevention suggest considering annual HCV Ab screening for individuals at high risk of infection [24], but the definition of "high risk" is vague.

Understanding current practices, as well as the rate of uptake of more routine screening for incident HCV infection, is essential to inform the development of evidence-based HCV screening strategies. We therefore used the Center for AIDS Research (CFAR) Network of Integrated Clinical Systems (CNICS) to investigate current and historical patterns of screening for HCV among HIV-infected individuals in the United States.

METHODS

Overview

We employed a retrospective cohort design to investigate the proportion of patients uninfected with HCV at entry into HIV care who ever received another HCV Ab or HCV RNA test after their negative baseline screening. We used bivariate and multivariate analyses to identify patient-level factors associated with more frequent screening, as well as factors associated with seroconversion. We analyzed calendar time trends to assess the screening rate for incident HCV after enrollment in care, and investigated the frequency of HCV diagnostic testing, using either HCV Ab or RNA, following elevated values of serum ALT.

Data Source

The CNICS cohort includes >29 000 HIV-infected adults in clinical care from 1995 to the present at 1 of 8 CFAR-funded sites including Case Western Reserve University; University of Alabama at Birmingham; University of California, San Francisco; University of California, San Diego; University of North Carolina at Chapel Hill; University of Washington; Johns Hopkins University; and Fenway Health in Boston [25] (available at: http://www.uab.edu/cnics). Seven CNICS sites contributed data to this analysis. Institutional review boards at each clinical site approved study protocols. For the purpose of result reporting, we name the sites by identification number only.

The CNICS data repository captures comprehensive clinical data, including standardized diagnoses, medications, laboratory, risk factors for HIV transmission, and demographic information collected through electronic health records and other institutional data systems at each site. Between 2006 and 2010, sites instituted a clinical assessment where patients use tablet computers to complete instruments measuring clinically relevant patient-related outcomes (PROs), including drug use and sexual risk behaviors every 4–6 months as part of routine clinical care visits. Data quality assessment is conducted at the sites prior to data transmission to the CNICS Data Management Core (DMC). All data are fully reviewed prior to quarterly integration into the repository with any quality issues investigated by the DMC. CNICS data elements relevant to this analysis included patient demographics, risk factors for HIV transmission, baseline CD4 cell count, history of AIDS-defining illnesses and of non-HCV liver disease at enrollment in care, self-reported amphetamine use and condom use, longitudinal laboratory results, and provider visit dates.

Participants and Screening Definitions

Participants for this analysis were ≥18 years of age who received an HCV Ab test within 3 months of entry into HIV care at a CNICS site ("baseline screening"). We limited the cohort to those with documented negative baseline screening to exclude those with prevalent HCV infection, as well as to exclude those who did not undergo baseline screening and whose HCV Ab testing may reflect "catch-up" to guidelines for screening for prevalent HCV at enrollment in care. Participants were required to have at least 12 months of follow-up time recorded in the dataset such that they were exposed to the "risk" of being screened for incident HCV. We defined all HCV Ab tests and HCV RNA tests subsequent to the baseline HCV Ab as "surveillance screening."

Follow-up Time Definitions

Participants began contributing follow-up time at their first visit in the dataset and continued to do so until either their last documented visit or laboratory test, whichever occurred last. For time trend analyses, we defined 3 distinct calendar periods of follow-up: 2000–2003, 2004–2007, and 2008–2011. We allowed participants to contribute time to ≥1 follow-up period as appropriate using a time-updated analysis.

Analysis of HCV Screening

We calculated the rate of surveillance HCV screening at each clinic site in each of the 3 calendar periods (defined as the total number of HCV Abs obtained at the site divided by the

Table 1. Characteristics of Included Participants (N = 9077) and Results of Multivariable Logistic and Poisson Regressions of Patient-Level Factors Associated With Surveillance Hepatitis C Virus (HCV) Antibody or RNA Screening Among HIV-Infected, HCV-Uninfected Patients

Characteristic	Participants, No. (Column %)	Ever Surveillance Screened vs Never, OR (95% CI)	Incidence Rate Ratio Surveillance Screens/PY, OR (95% CI)
Follow-up time, y			
Mean	4.85		
Median	4.11		
Range	1–12.3		
Calendar period			
2000–2003			Ref.
2004–2007			1.82 (1.68–1.97)
2008–2011			2.30 (2.01–2.49)
Age, y			
<20	79 (0.9)	Ref.	Ref.
20–39	5111 (56.3)	0.88 (.53–1.45)	0.97 (.78–1.29)
40–59	3698 (40.7)	0.68 (.41–1.13)	0.86 (.68–1.07)
>60	189 (2.1)	0.55 (.31–1.00)	0.83 (.63–1.09)
Sex			
Female	1421 (15.6)	Ref.	Ref.
Male	7656 (84.3)	1.09 (.92–1.29)	1.06 (.99–1.14)
Race			
White	5176 (57.0)	Ref.	Ref.
Black	2791 (30.7)	1.11 (.99–1.26)	1.00 (.95–1.06)
Other	829 (9.1)	0.88 (.75–1.03)	0.96 (.90–1.03)
Unknown	281 (3.1)		
Risk factor for HIV transmission			
IDU	195 (2.1)	Ref.	Ref.
MSM	5778 (63.7)	0.59 (.42–.84)	0.80 (.70–.91)
MSM/IDU	504 (5.6)	1.13 (.75–1.71)	1.0 (.86–1.16)
Heterosexual	2277 (25.1)	0.513 (.36–.73)	0.76 (.66–.87)
Other	323 (3.56)	0.55 (.36–.73)	0.75 (.64–.89)
History of AIDS-defining illness at enrollment			
Yes	3007 (33.1)	1.16 (1.04–1.31)	1.0 (.93–1.08)
No	6070 (66.9)		
History of non-HCV liver disease			
Yes	302 (3.3)	3.41 (2.51–4.63)	1.03 (.98–1.08)
No	8775 (96.7)		
CD4 count at enrollment, cells/μL			
<50	1205 (13.3)	Ref.	Ref.
50–99	562 (6.2)	0.86 (.42–.84)	0.91 (.82–1.00)
100–199	1060 (11.7)	0.93 (.76–1.13)	0.93 (.86–1.01)
200–349	1798 (19.8)	1.02 (.86–1.22)	0.97 (.90–1.04)
350–499	1783 (19.6)	1.08 (.90–1.29)	1.01 (.93–1.09)
≥500	2668 (29.4)	1.09 (.92–1.30)	1.00 (.93–1.08)
Missing	1 (0.01)		
Patient-reported amphetamine use			
No use	2235 (24.6)	Ref.	Ref.
Past use	1052 (11.6)	1.12 (.94–1.35)	1.0 (.93–1.07)
Current use	454 (5.0)	1.86 (1.42–2.44)	1.26 (1.14–1.38)
Unknown	5336 (58.8)	0.72 (.51–1.01)	0.84 (.71–1.0)
Patient-reported condom use for anal sex			
No anal sex	1847 (20.4)	Ref.	Ref.
Always	601 (6.6)	1.14 (.92–1.42)	0.98 (.90–1.08)
Inconsistent	1116 (12.3)	1.31 (1.08–1.59)	1.09 (1.01–1.17)
Unknown	5531 (60.7)	1.40 (.69–2.87)	1.28 (1.01–1.64)
Patient-reported condom use for vaginal sex			
No vaginal sex	2964 (32.7)	Ref.	Ref.
Always	337 (3.7)	0.96 (.73–1.26)	0.97 (.87–1.09)
Inconsistent	241 (2.7)	1.31 (1.08–1.59)	1.24 (1.10–1.40)
Unknown	5535 (61.0)	1.40 (.69–2.87)	1.06 (.85–1.33)
Clinical site			
1	1463 (16.1)	Ref.	Ref.
2	777 (8.6)	0.99 (.79–1.23)	1.24 (1.10–1.39)
3	1642 (18.1)	9.57 (7.88–11.61)	1.37 (1.24–1.50)
4	2235 (24.6)	4.31 (3.66–5.08)	2.08 (1.92–2.26)
5	980 (10.8)	1.86 (1.52–2.29)	1.07 (.97–1.19)
6	1254 (13.8)	0.86 (.72–1.04)	1.70 (1.54–1.87)
7	726 (8.0)	3.20 (2.58–3.97)	2.63 (2.42–2.85)

Abbreviations: CI, confidence interval; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IDU, injection drug use; MSM, men who have sex with men; OR, odds ratio; PY, person-year; Ref., reference group.

total person-years of follow-up). Next, we calculated the rate of surveillance screening for each individual (defined as the number of HCV Ab obtained for a given individual/the individual's follow-up) and the median rate of screening stratified by clinic site. We reported the proportion of patients at each site who had received at least 1 surveillance screening test (Ab or RNA) at fixed time intervals, while censoring patients who were lost to follow-up at each time point.

Analysis of Response to Elevated ALT

For each participant, we identified the first ALT result (if any) that was >40 IU/L (the upper limit of normal). We stratified these first-observed elevated results by degree of elevation (41–100 IU/L, 101–400 IU/L, >400 IU/L) and reported the percentage of time that a first-observed elevated ALT was followed by diagnostic HCV Ab and RNA testing within 3, 6, and 12 months. If a participant had >1 ALT value >40 IU/L, we included only the first value >40 IU/L, such that participants with multiple elevated ALT levels were only considered once. We included patients who had a baseline ALT >40 IU/L in the analysis, because if one is using ALT as a screening test for incident HCV, the first-ever observation of an elevated ALT likely should be followed with HCV diagnostic testing. As we included only the first instance of elevated ALT, subsequent elevations were not

included in the analysis. In addition, because European guidelines recommend routine ALT screening only for HIV-infected MSM [22], we repeated the analysis, including only participants who reported MSM as their HIV transmission risk factor.

Statistical Methods

We used Pearson χ^2 test, Student *t* test, and multivariate logistic regression to investigate differences in patient-level characteristics among those who received at least 1 surveillance HCV screening and those who were screened at baseline only. Next, we used χ^2 test and logistic regression to compare patient-level factors associated with seroconversion. We then used multivariate Poisson regression, in which the number of surveillance HCV screens was the outcome of interest with the time of follow-up as an offset variable, to identify patient-level factors associated with more frequent surveillance screening. Covariates in multivariable models included follow-up time contributed, age, sex, race, history of AIDS-defining illness, history of non-HCV liver disease, risk factors for HIV transmission (MSM, IDU, MSM/IDU, heterosexual, or other), patient-reported amphetamine use and condom use, and clinic site. The "other" category includes those who reported hemophilia/coagulation disorders, receipt of blood transfusion, perinatal infection, and healthcare workers. Because PROs were not available at all sites throughout follow-up, we maintain "unknown" as a separate category for all multivariable models. In addition, we performed a sensitivity analysis limiting the cohort to those who enrolled at CNICS sites during a time period when PROs were being collected. Significance was set at $P < .05$ for all analyses, and all statistical testing was conducted using Stata software version 12.0 (StataCorp LP, College Station, Texas).

RESULTS

Cohort Characteristics

There were 17 090 CNICS participants ≥18 years of age seen at least once during 2000–2011. Of these, 16 002 (93.6%) were screened with HCV Ab at least once during follow-up, and 14 534 (85%) were screened within 3 months of their first clinical visit (baseline screening). Among those who received baseline screening, 2275 (15.6%) were excluded from this analysis because they had reactive HCV Ab, yielding 12 259 CNICS participants with nonreactive HCV Ab at baseline. Of those, 3182 were excluded because they had <1 year of follow-up. In total, 9077 participants met all inclusion criteria (Table 1). Participants included in the analysis were similar in demographic characteristics to the general CNICS cohort.

Analysis of Surveillance HCV Screening

Among the 9077 participants included in the analysis, 5042 (55.6%) had at least 1 surveillance HCV Ab or RNA screening test. In bivariate analysis, the proportion of patients who ever had surveillance HCV Ab or RNA screening varied significantly by clinical site, ranging from 35.3% at site 1 to 78.5% at site 3. In multivariate logistic regression adjusting for time of follow-up, participants who reported inconsistent condom use during anal sex were significantly more likely to receive surveillance HCV screening than those who reported not having anal sex (odds ratio [OR] = 1.31 [95% confidence interval {CI}, 1.08–1.59]; Table 1). Similarly, those who reported current amphetamine use were more likely to be screened than those who reported no amphetamine use (OR = 1.86 [95% CI, 1.42–2.44]; Table 1). Clinical traits associated with greater odds of HCV surveillance screening included baseline history of AIDS-defining illness

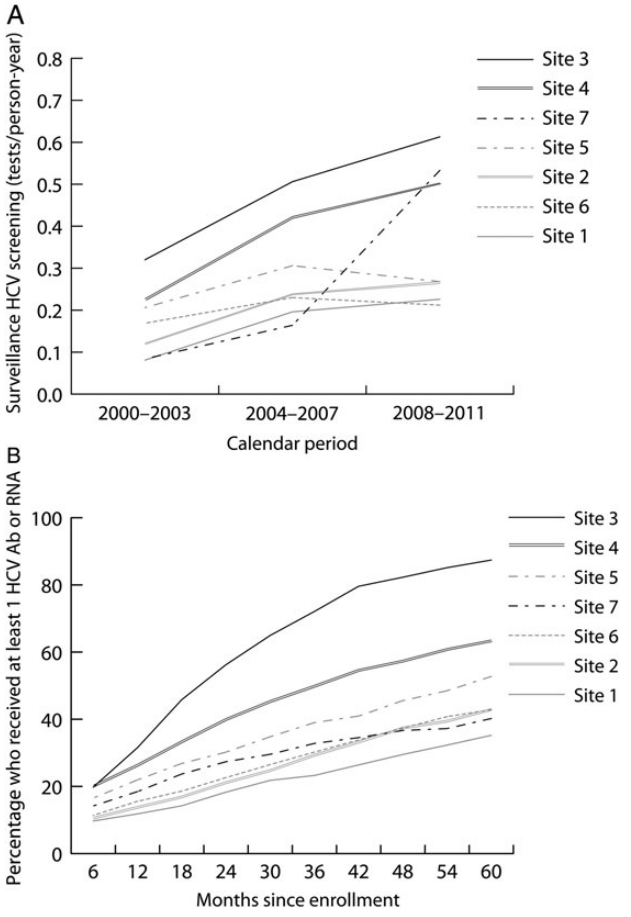

Figure 1. Rates of surveillance screening for incident hepatitis C virus (HCV) infection among human immunodeficiency virus-infected, HCV-uninfected individuals enrolled at 7 Center for AIDS Research Network of Integrated Clinical Systems sites from 2000 to 2011. *A,* Incidence of screening for HCV across the entire clinic population (calculated as the total number of HCV antibody [Ab] or RNA tests/total person-time of follow-up). *B,* Cumulative incidence of first-time surveillance screening test for incident HCV infection at each clinical site. In this analysis, participants were censored when lost to follow-up.

Table 2. Associations Between Clinical and Behavioral Characteristics and Development of Incident Hepatitis C Virus (HCV) Among HIV-Infected, HCV-Uninfected Participants, 2000–2011 (n = 267)

Characteristic	Odds Ratio (95% CI)	*P* Value
Age, y		
<20	Ref.	
20–39	1.04 (.24–4.58)	.96
40–59	0.74 (.17–3.27)	.69
>60	0.64 (.10–4.30)	.65
Sex		
Male	Ref.	
Female	1.19 (.74–1.89)	.47
Race		
White	Ref.	
Black	1.12 (.80–1.56)	.53
Other	0.88 (.59–1.33)	.54
Risk factor for HIV transmission		
IDU	Ref.	
MSM	0.25 (.15–.45)	<.001
MSM/IDU	0.82 (.45–1.51)	.42
Heterosexual	0.19 (.1–.34)	<.001
Other	0.41 (.19–.88)	.023
CD4 cell count, cells/μL		
<50	Ref.	
50–99	1.08 (.53–2.20)	.83
100–199	1.59 (.91–2.76)	.10
200–349	1.51 (.90–2.54)	.12
350–499	0.91 (.52–1.59)	.73
≥500	1.34 (.80–2.24)	.26
History of AIDS-defining illness	1.00 (.74–1.36)	.99
History of non-HCV liver disease	2.71 (1.72–4.28)	<.001
Patient-reported amphetamine use		
No use	Ref.	
Past use	1.86 (1.12–3.08)	.02
Current use	3.59 (2.07–6.21)	<.001
Unknown	1.59 (.70–3.59)	.27
Patient-reported condom use for anal sex		
No anal sex	Ref.	
Always	1.19 (.61–2.33)	.61
Inconsistent	1.59 (.98–2.56)	.06
Unknown	0.35 (.09–1.42)	.14
Patient-reported condom use for vaginal sex		
No vaginal sex	Ref.	
Always	0.50 (.15–1.67)	.26
Inconsistent	1.85 (.93–3.67)	.08
Unknown	3.75 (1.09–12.89)	.04
Clinical site		
1	Ref.	
2	0.43 (.15–1.23)	.12
3	1.74 (.95–3.17)	.07
4	1.16 (.64–2.08)	.63
5	0.98 (.47–2.01)	.95
6	1.63 (.86–3.08)	.13
7	1.33 (.66–2.71)	.43

Table 2 continued.

Abbreviations: CI, confidence interval; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IDU, injection drug use; MSM, men who have sex with men; Ref., reference group.

(OR = 1.16 [95% CI, 1.04–1.31]) and having a history of non-HCV liver disease (OR = 3.41 [95% CI, 2.51–4.63]). Those who reported MSM or heterosexual as their risk factor for HIV transmission were less likely than IDU to ever receive surveillance HCV screening (OR = 0.59 [95% CI, .42–.84] and OR = 0.513 [95% CI, .36–.73], respectively). The clinical site at which participants received care was a significant predictor of the odds of receiving surveillance HCV screening and had larger effect estimates than reported risk for HIV transmission. The odds of ever receiving HCV surveillance at site 3 were 9.6 times greater (95% CI, 7.88–11.61) than those at site 1 (Table 1). When we limited the cohort to those enrolled in sites collecting PRO data, clinical site continued to have a larger effect on surveillance screening than did patient risk behaviors.

Across the follow-up period, the rate of surveillance HCV Ab and RNA screening varied significantly by site, ranging from 0.14 to 0.52 screens per person-year. Surveillance screening increased over time, but the rate of increase differed between sites (Table 1; Figure 1*A* and 1*B*). In the most recent calendar period (2008–2011), the screening rates ranged from 0.24 at site 1 to 0.63 at site 3. In multivariate analysis that controlled for patient demographics, risk factors for HIV transmission, clinical characteristics, drug use and sexual risk behaviors, clinical site, and calendar time, the surveillance screening rate varied significantly between sites (Table 1).

When we considered the median individual screening rate, we observed similar trends. At the beginning of the follow-up period, the median rate of screening at all sites was zero. Over time, the median rate of screening increased at most sites, but not all. Between 2008 and 2011, the median rate of screening remained zero at sites 1 and 6, meaning that at least 50% of the participants at those sites were never screened for HCV after their negative baseline screen. At site 3, the site with the highest rates of screening, the median rate of screening was 0.55, meaning that 50% of patients were screened for incident HCV at least once every 2 years.

Additionally, the proportion who had received surveillance screening at fixed time intervals had similar variation in screening between sites. For example, among those who were followed for 60 months at site 3, 87% had received at least 1 surveillance HCV test by month 60, whereas among those followed for

Table 3. Rates of Diagnostic Hepatitis C Virus (HCV) Antibody or RNA Testing in Response to Elevated Alanine Aminotransferase Levels Among All HIV-Infected, HCV-Uninfected Participants and Among HIV-Infected, HCV-Uninfected Men Who Have Sex With Men

ALT Value, IU/L	Total No.	Diagnostic HCV Ab or RNA Within 3 mo		6 mo		12 mo	
		No.	%	No.	%	No.	%
All participants							
41–100	3143	250	7.9	362	11.5	571	18.2
101–400	509	78	15.3	100	19.7	136	26.7
>400	79	12	15.2	13	16.5	16	20.3
Total	3731	340	9.1	475	12.7	723	19.4
MSM only							
41–100	2294	179	7.8	268	11.7	432	18.8
101–400	360	60	16.7	73	20.3	101	28.1
>400	61	8	13.1	8	13.1	11	18.0
Total	2715	247	9.1	349	12.9	544	20.0

Abbreviations: Ab, antibody; ALT, alanine aminotransferase; HCV, hepatitis C virus; MSM, men who have sex with men.

60 months at site 1, 35% had been screened. When we restricted the analysis to MSM only, we found rates similar to those observed in the cohort as a whole and similar pattern in screening trends over time. At sites 3, 5, and 7, rates of screening among HIV-infected MSM increased substantially compared with other sites (Figure 1*B*).

Analysis of Seroconversion and Factors Associated With Seroconversion

Among the 5042 participants who had at least 1 surveillance HCV screening test performed, 267 (5.3%) seroconverted. The mean ALT level prior to positive HCV testing was 101.7 (95% CI, 82.8–120.8), and median ALT was 61.5 IU/L (interquartile range, 45.5–77.6). Participants who seroconverted were more likely to report past or current amphetamine use (OR = 1.86 [95% CI, 1.12–3.08] for past use, and OR = 3.59 [95% CI, 2.07–6.21] for current use). Inconsistent condom use (anal or vaginal sex) was associated with seroconversion, but the finding did not meet the level of statistical significance. Seropositivity was also higher among MSM/IDU than among the MSM or heterosexual risk categories (OR = 0.82 [95% CI, .45–1.51]; Table 2).

Analysis of Response to Elevated ALT Levels

There were 3731 first-time ALT results >40 IU/L (Table 3). Among the entire cohort, 26.7% of ALT levels >100 IU/L and 20.3% of ALT >400 IU/L were followed with HCV Ab or RNA testing within 12 months of the first-time elevated ALT result. When we considered only elevated ALT results among MSM, 28.1% of ALT elevations >100 IU/L and 18.0% of ALT >400 IU/L were followed by diagnostic HCV Ab testing within 12 months.

DISCUSSION

This analysis demonstrates that although the large majority of HIV-infected patients in the United States are screened for HCV at enrollment in care, among those who do not have prevalent infection at baseline, surveillance screening for incident HCV infection varies substantially between clinical sites—even among those who report high-risk characteristics such as current amphetamine use and anal sex with inconsistent condom use. In multivariate analysis, the site at which a subject receives care has a larger impact than HIV transmission risk factors and PROs on both the odds of ever receiving surveillance screening and the rate of surveillance screening. Although some sites have increased the frequency of screening for HCV, the rate of change over calendar time is variable. Furthermore, fewer than one-third of ALT levels >100 IU/L are followed-up with diagnostic HCV Ab testing within 12 months of the elevated result.

Screening for incident HCV is variable across sites and improvement in frequency of screening is also variable, highlighting a need for US-based guidelines to inform HIV practice. Such guidelines exist for one-time screening for prevalent HCV infection among HIV-infected patients [26], resulting in >90% of participants receiving at least 1 HCV Ab screening and 85% screened for HCV within 3 months of enrolling in care. Although publishing a recommendation for frequent and routine HCV screening will not itself change clinical practice, doing so would encourage providers to screen routinely and provide a metric by which practices could measure their performance. This analysis does not include processes of care at specific sites that may have influenced the increase in screening rates, and future studies to understand uptake, spread, and variability in provider practice may help success of such guideline implementation.

European HCV screening guidelines currently recommend routine screening for incident HCV among HIV-infected MSM using serum ALT every 6 months combined with HCV Ab every 12 months [22]. The positivity threshold that should trigger additional diagnostic testing, however, is not clear. ALT is an attractive screening test of incident HCV, because current antiretroviral therapy guidelines already recommend ALT monitoring every 6 months to assess treatment toxicity [27]. Mathematical modeling studies suggest that such a strategy would extend life expectancy and be cost-effective [23]. However, our analysis demonstrates that among HIV-infected MSM, fewer than one-third of first-time ALT values >100 IU/L were followed up with diagnostic HCV Ab or RNA testing. Thus, it

appears that providers in the United States do not routinely use ALT as a screening test for incident HCV.

Certainly, there are many clinical explanations for an elevated ALT, and providers who know that their patient has a noninfectious etiology for an elevated ALT would likely not follow every elevated value with diagnostic HCV testing. We limited our analysis, however, to only first-time ALT elevations, and still found that less than one-third were followed with a diagnostic evaluation for HCV infection. It is very unlikely that 70% of first-time elevated ALT levels >100 IU/L were completely explained by other comorbidities. If US guidelines recommend more frequent screening for HCV using ALT, future work will need to define a clear threshold.

There are limitations to this analysis. First, residual confounding could obscure the fact that observed differences in screening rates among clinical sites reflect differences in patient populations, rather than practice variation based predominantly on geography. We used patient-reported drug use and condom use behaviors to control for differences in HCV risk; such self-reported behaviors may be biased. In addition, because CNICS data are extracted from medical records, it is possible that some patients in the cohort received a portion of their care at a non-CNICS center, resulting in incomplete outcomes data.

In summary, this analysis demonstrates that although most HIV-infected patients are screened once for prevalent HCV infection at entry into HIV care, significant practice variations remain in rates of screening for incident HCV. These differences are not well explained by patient demographics or risk behaviors, although patients who report IDU remain more likely to be screened than MSM or heterosexual patients. Additionally, those with new ALT elevations to >100 IU/L are unlikely to have diagnostic testing for HCV. Therefore, opportunities exist to improve outcomes; US-based national guidelines informing whom to screen, how frequently to screen them, and what screening test to use are an important first step in this direction.

Notes

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